

Protocol for the use of intramuscular (IM) clozapine injection

Key Points for Consideration:

1. Clozapine injection is not licensed for use in the UK.
2. The Trust has approved its use, in exceptional circumstances, for patients in PICUs and secure units ONLY.
3. Clozapine injection can only be obtained by following this protocol. Other methods / routes of obtaining it are not available.
4. Clozapine injection can only be prescribed if approved by a SOAD.
5. It can only be prescribed by a consultant and use of the product must be approved by the Clinical Director on an individual patient basis.
6. Clozapine injection is expensive. Dose titration over 2 weeks costs £2,000

What is IM clozapine?

Intramuscular clozapine is an unlicensed product made in the Netherlands by Brocacef and imported to the UK via Durbin PLC. It is a clear yellow solution for injection. The strength of the injection is 25mg/ml and each ampoule contains 5mls (125mg). It is administered by deep intramuscular injection into the gluteal muscle. The injection is painful and the maximum volume that can be injected into each site is 4ml (100mg). For doses greater than 100mg daily (beyond the scope of this protocol), the dose may be divided and administered into two sites. (Injection sites should be rotated as per usual IM practice).

What is the objective of using IM clozapine?

Clozapine injection is a short-term intervention to initiate clozapine in patients with treatment-resistant schizophrenia who refuse oral clozapine, with a view to convert to oral clozapine as soon as possible. It should only be used when all other approaches have failed and only in those who are predicted to respond to clozapine treatment.

Who can have IM clozapine?

Clozapine injection may only be prescribed and administered on the direct written authority of the Chief Pharmacist – (Governance & Professional Practice):

jed.hewitt@sussexpartnership.nhs.uk.

All requests must also be signed off by the clinical director.

The injection is indicated only for patients with a treatment-refractory psychotic disorder who are refusing oral clozapine treatment. It can be used for patients who have never been exposed to clozapine previously or patients previously treated with clozapine and known to have responded but relapsed owing to non-adherence. The need for clozapine injection must be agreed by the MDT, approved by the SOAD, and fully documented in Carenotes using the bespoke assessment form (see appendix 1).

Use must be requested on an individual patient basis only and is only approved for use in PICUs and secure units.

Registration of patients for IM clozapine

All patients for IM clozapine must be registered with the Clozaril Patient Monitoring Service (CPMS) as the objective is to use the injection for the shortest possible time before switching to oral treatment. After treatment with clozapine injection has been agreed by the MDT and approved by the SOAD, (also the Chief Pharmacist and Clinical Director), the CPMS must be informed of the treatment plan and the patient registered accordingly. The usual clozapine mandatory baseline and weekly blood monitoring and the necessary precautions for amber and red warnings all apply.

How long can the treatment continue for?

Clozapine injection should be used for the shortest duration possible. Before administering each injection, the patient should be offered oral clozapine. The need for ongoing IM treatment must be reviewed regularly by the MDT. In general, the injection should be used for no longer than two weeks. In exceptional cases, the injection may be used for longer, if approved by the MDT, SOAD, Clinical director, and Chief Pharmacist.

How is IM clozapine obtained?

Clozapine injection will not be held as stock on any Trust units. It can only be obtained for named-patients against a special order and will normally take two weeks to arrive in pharmacy from the time of ordering.

What is the oral equivalent of the IM?

The oral bioavailability of clozapine is about half that of the intramuscular injection. For example, 50mg daily of the IM injection is roughly equivalent to 100mg daily of the tablets. If the patient switches to or from IM clozapine during titration, the dose prescribed and administered must be adjusted accordingly.

Starting clozapine injection

The patient must be registered with CPMS the week before commencing treatment. Treatment should start on a Monday whenever possible. Clozapine should be prescribed on the main drug chart and annotated 'see separate clozapine titration sheet'. Each dose on the titration sheet must be signed and dated by the prescriber. The **clozapine injection prescription chart**, (see appendix 3), must be attached to the main drug chart. The patient should always be offered oral clozapine first, before any IM clozapine injection is prepared, and if the patient continues to refuse, then the injection can be administered. **Nursing staff must clearly indicate the route of administration used on the titration sheet, which has oral and IM equivalent doses specified.**

Consideration must be given to other medication currently prescribed. Other antipsychotics should be reduced and the total BNF cumulative dose should not exceed 100%.

Monitoring of patients on IM clozapine treatment

Baseline assessment before starting clozapine must include ECG, FBC, lipids, plasma glucose, U&Es, LFT, CRP and troponin.

Intramuscular Clozapine Injection MDT Assessment Form.

Name of Patient	
Date of birth	
CIS ID number	
Indication for clozapine	
Date patient registered with CPMS	
Any significant physical health comorbidities that might contra-indicate the use of clozapine?	
Has patient previously been prescribed clozapine? If yes, state reason clozapine was stopped previously	
Date of SOAD approval	
Date MDT discussion documented in clinical notes	
Name of Consultant	
Signature of Consultant	
Name of Clinical Director approving treatment	
Signature of Clinical Director approving treatment	
Date request received by Chief Pharmacist	
Chief Pharmacist approval signature	

Tasks to be undertaken prior to commencing IM clozapine treatment

Patient name: DoB: CIS ID:

Task	Date	Recorded in Care notes	Comments
Fully complete the MDT assessment form and necessary approval			
Register patient with CPMS			
Order IM clozapine via pharmacy (Can take 1-2 weeks).			
Doctor discussion with patient regarding IM administration.			
Ward pharmacist discussion with patient regarding IM administration. Patient information leaflet given.			
Baseline assessments completed: ECG, FBC, lipids, plasma glucose, U&Es, LFT, CRP and troponin			
Review of antipsychotics (including clozapine) and calculation of %BNF total. (Should be below 100%).			
Ward pharmacist discussion with nursing staff regarding dosage and administration issues.			
MDT discussion regarding PMVA techniques.			
MDT discussion regarding daily monitoring of BP, pulse, respiratory rate and temperature.			
Prescription written on drug chart and on supplementary chart.			
Preparation of monitoring form.			
Ward pharmacist screen of initial prescription and all medication.			
Ward pharmacist check of blood results & supply of IM clozapine arranged.			

CLOZAPINE INJECTION PRESCRIPTION CHART**ALWAYS OFFER ORAL CLOZAPINE FIRST**

Ward		Hospital/Unit	
Patient Name		CPMS Number	
Consultant		Hospital No.	
Allergies		Date of birth	

❖ **CAUTION: IM CLOZAPINE DOSE IS ONLY HALF THE ORAL DOSE**❖ **CAUTION: ONLY FOR IM ADMINISTRATION INTO GLUTEAL MUSCLE**

Day	Date	Oral Dose ALWAYS OFFER FIRST BEFORE USING IM.	IM Clozapine (25mg/ml) ONLY USE IF ORAL DOSE REFUSED	Prescriber's signature	Specify route given (PO or IM) If IM state side given (L) or (R) & site	Given by
1		12.5mg	6.25mg (0.25ml)			
2		25mg	12.5mg (0.5ml)			
3		25mg	12.5mg (0.5ml)			
4		50mg	25mg (1ml)			
5		50mg	25mg (1ml)			
6		75mg	37.5mg (1.5ml)			
7		75mg	37.5mg (1.5ml)			

Note: The clozapine injection must also be prescribed on the inpatient drug chart and be cross-referenced to this titration sheet. Clozapine injection must be prescribed by consultant only.

Continued overleaf.

Week Two.

ALWAYS OFFER ORAL CLOZAPINE FIRST

- ❖ CAUTION: IM CLOZAPINE DOSE IS ONLY HALF THE ORAL DOSE
- ❖ CAUTION: ONLY FOR IM ADMINISTRATION INTO GLUTEAL MUSCLE

Day	Date	Oral Dose ALWAYS OFFER FIRST BEFORE USING IM	IM Clozapine (25mg/ml) ONLY USE IF ORAL DOSE REFUSED	Prescriber's signature	Specify route given (PO or IM) If IM state side given (L) or (R) & site	Given by
8		100mg	50mg (2ml)			
9		100mg	50mg (2ml)			
10		125mg	62.5mg (2.5ml)			
11		125mg	62.5mg (2.5ml)			
12		150mg	75mg (3ml)			
13		150mg	75mg (3ml)			
14		175mg	87.5mg (3.5ml)			

Note: The clozapine injection must also be prescribed on the inpatient drug chart and be cross-referenced to this titration sheet. Clozapine injection must be prescribed by consultant only.

Additional notes.

CLOZAPINE INJECTION PHYSICAL OBSERVATIONS CHART

(Please see instructions on back)

Patient name		Ward		Date of birth												
DATE	Time monitoring initiated:			Time monitoring stopped:												
TIME (24 hour)		MEWS														
Observations (minutes)	0	15	30	45	60	75	90	105	120	135	150	165	180	195	210	
Temperature 36.1 - 37.4 °C	40									40	3					
	39									39	3					
	38.5									38.5	3					
	38									38	3					
	37.5									37.5	2					
	37									37	0					
	36									36	0					
	35									35	1					
34									34	3						
Temperature		Temperature														
SYSTOLIC Blood Pressure (100-139)	≥200	3								≥200	3					
	190	2								190	3					
	180	2								180	3					
	170	2								170	3					
	160	1								160	3					
	150	1								150	3					
	140	1								140	3					
	130	0								130	3					
	120	0								120	3					
	110	0								110	3					
	100	0								100	3					
	90	1								90	2					
	80	1								80	0					
	70	3								70	0					
60	3								60	0						
50	3								50	2						
40	3								40	3						
Systolic BP		Diastolic BP														
Pulse (51 - 100)	140 >									140	3					
	130									130	3					
	120									120	3					
	110									110	2					
	100									100	1					
	90									90	0					
	80									80	0					
	70									70	0					
	60									60	0					
	50									50	1					
40									40	3						
Pulse		Pulse														
Respirations (12 - 20)	≥ 30									≥ 30	3					
	21-29									21-29	2					
	17-20									17-20	0					
	12-16									12-16	0					
	10-11									10-11	1					
	9									9	2					
≤ 8									≤ 8	3						
Respirations		Respirations														
SPO ₂	97-100									97-100	0					
	94-96									94-96	0					
	≤ 93									≤ 93	3					
Oxygen Saturation		Oxygen Saturation														
Conscious Level	Awake and active									A	0					
	Awake and calm									A	0					
	Asleep but rousable									R	2					
	Asleep and Unresponsive									U	3					
Conscious Level		Conscious Level														
Hydrated-Yes(0)or No(2)		Hydrated														
TOTAL MEWS		TOTAL MEWS														
Signature/Initials		Signature/initials														

If patient is ambulatory and stable, carry out MDT review to consider discontinuing observations.

Instructions:

- Use this chart to record patient monitoring undertaken during a single episode of intramuscular (IM) clozapine
- If patient consents to physical examinations, ALL observations on this chart should be recorded.
- If patient refuses observations, record as **R**. **Respiration rate** and **consciousness** should still be recorded.
- Monitor at least every 15 **minutes**
- Continue monitoring for a minimum of **120 minutes** and longer if the patient remains unstable.